Considerations for FDA Licensure vs. Emergency Use Authorization of COVID-19 Vaccines

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FDA Licensure

- **Requirement for demonstration of vaccine safety, effectiveness and controlled/consistent manufacturing to ensure continued safety and effectiveness of the licensed vaccine**

- **“Traditional” approval pathway for COVID-19 vaccines**
  - Substantial evidence of effectiveness to support licensure could be demonstrated in clinical disease endpoint efficacy trials

- **Other FDA licensure pathways (accelerated approval, “animal rule”) would not apply to COVID-19 vaccines at this time, given:**
  - Sufficient COVID-19 incidence to allow for clinical disease endpoint efficacy trials
  - Limited understanding of SARS-CoV-2 immunology and immune response biomarkers that might predict protection against COVID-19

Considerations for licensure

- **Efficacy is necessary, but not sufficient**
  - A large efficacy trial conducted in areas of high disease activity may rapidly accrue enough cases to achieve the specified efficacy success criterion before availability of other data to inform benefit-risk considerations for review of a licensure application:
    - Longer-term safety data
    - Data to support manufacturing processes, facilities, product characterization, and demonstration of lot-to-lot consistency

Considerations for licensure

- **Licensure application review process must address statutory and regulatory requirements for approval**
  - Review of complex clinical, nonclinical, and manufacturing data
  - Information requests and meetings with applicant to resolve issues
  - Facilities and clinical trial site inspections
  - Safety update with longer-term safety data
  - Pharmacovigilance plan
  - Plans to satisfy pediatric study requirements
  - External scientific advisory committee input (VRBPAC), as needed

Emergency Use Authorization (EUA)

- **Qualifying Criteria:**
  - Declaration by HHS Secretary of emergency situation leading to serious or life-threatening disease or condition
  - Evidence of effectiveness for product intended to address emergency
    - EUA standard: “may be effective”
  - Known and potential benefits of the product outweigh the known and potential risks of the product
    - Intended use (e.g., number of individuals to be treated) and risk uncertainties impact application of EUA effectiveness standard
  - No adequate, approved, and available alternative

Emergency Use Authorization (EUA)

- **Requested by government stakeholder (e.g., CDC, BARDA, DoD) or manufacturer; materials submitted to FDA include, but not limited to:**
  - Specific details of requested product use under EUA: population, dose, regimen
  - Supportive safety, effectiveness, and manufacturing information
  - Fact sheets for patients and healthcare providers
- **Regulations and law allow for more rapid review vs. licensure application**
- **Conditions of authorization:**
  - Monitoring and reporting adverse events required “to the extent practicable”
  - Duration of authorization specified, can be renewed or terminated early
  - Other conditions, as applicable (e.g., distribution, advertising)

Considerations for EUA

- **FDA Guidance for Industry: Development and Licensure of Vaccines to Prevent COVID-19 (June 2020):**
  - Issuance of an EUA based on very preliminary safety and efficacy data from randomized, controlled trials could reduce the ability to demonstrate effectiveness and assess benefits vs. risks of the vaccine to support licensure
  - For a vaccine for which there is adequate manufacturing information, issuance of an EUA may be appropriate once studies have demonstrated the safety and effectiveness of the vaccine but before the manufacturer has submitted and/or FDA has completed its formal review of the biologics license application
  - Any assessment regarding an EUA would be made on a case by case basis considering the target population, characteristics of the product, preclinical and human clinical study data, and the totality of available relevant scientific evidence

Resources

- **FDA Guidance for Industry: Development and Licensure of Vaccines to Prevent COVID-19**
  - https://www.fda.gov/media/139638/download

- **FDA Guidance for Industry and Other Stakeholders: Emergency Use Authorization of Medical Products and Related Authorities**
  - https://www.fda.gov/media/97321/download

- **FDA EUA Website**
  - https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization